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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,584	08/25/2003	Arthur M. Krieg	C1039.70084US00	5262

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EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/649,584	KRIEG ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,87 and 88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,87 and 88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 10/31/07. Claims 1, 2, 87 and 88 are pending in this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 87 and 88 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering an unmethylated CpG nucleic acid wherein the CpG nucleic acid is an adjuvant nucleic acid administered in the presence of a vaccine to a subject infected with an immune deficiency associated with HIV to induce an immune response to the vaccine and wherein the method does not treat HIV does not reasonably provide enablement for any other embodiment.. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. **This is a new rejection necessitated by applicants' amendment.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without

undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention**. The instant claims are drawn to a method for treating a subject by administration of *any* subject with an immune system deficiency associated with HIV infection by administration of *any* unmethylated CpG nucleic acid with the express purpose of boosting the subject's immune system.

2) Scope of the invention. The scope of the invention is quite broad even though in dependent claim 2 the nucleic acid is limited to one that does not include a palindrome and claim 87 such that B and/or NK cells are stimulated and claim 88 that the CpG is administered with a vaccine.

3) Number of working examples and guidance. The specification teaches design of several types of CpG molecules, immunostimulatory, adjuvant and IFN-α inducing molecules. With regard to adjuvant nucleic acids, the specification teaches that these nucleic acids would mediate response that would function to boost a subject's response to a vaccine and provide several examples of such sequences and assay the immunostimulating activity of these molecules. However, the specification does not disclose the type of vaccine to be used with the nucleic acids nor does it demonstrate use of the nucleic acid as an adjuvant. Applicants have attempted to define an adjuvant type molecule in by introduction of SEQ ID NO:s 27-72 in 09/931,853. SEQ ID NO:27-34 are presented as models for sequences that function as adjuvant

CpG molecules with model sequences (SEQ ID NO:27 and 28) 5'-TCN_1TN_2 $X_1X_2CGX_3X_4$-3' and 5'-TCN_1T $X_1X_2CGX_3X_4$-3'. With regard to IFN-α inducing nucleic acids, applicants propose two sequences again introduction in parent application 09/931,583 upon which the IFN-a inducing nucleic acids are based. The specification continues that IFN-α-inducing CpG nucleic acid comprise SEQ ID NO:73, 5'-$Y_1N_1X_2CGX_3X_4$ N_2 Y_2.3' as the model sequences but also teach that SEQ ID NO:30 functions specifically as one such molecule. SEQ ID NO:29 and 35-72 function as immunostimulatory molecules where as the model immunostimulatory nucleic acid is presented by the formula of 5'-$X_1X_2CGX_3X_4$-3'. The functionality of the disclosed sequences is demonstrated by administration of SEQ ID NO:s 2, 5, 6, 7, 8, 11, 13-15, 18, 21, 26 and TCAACGTT to uninfected mice resulting in enhanced IgM production, natural killer cells and IL-6. Based solely on the above observations, applicants have proposed use of CpG unmethylated nucleic acids to treat HIV. Specifically, in the instant claims, applicants propose use of the CpG nucleic acids to boost the immune system of a subject with an immune deficiency associated with an HIV infection.

4) **State of Art**. In the instant case, the claims are extremely broad and based upon a reading of the specification are directed toward treatment of a subject with HIV infection. HIV is a virus known to infect humans. The response to HIV infection is multifaceted and complex often resulting in AIDS. Current guidelines have established that the goal in medical management of HIV infection and AIDS is maximal suppression of HIV replication. To do so, triple therapy is recommended starting with protease inhibitor. By inhibiting viral load at initial infection emergence of drug resistant strains can be avoided (see e.g. De Cock, page 1, ¶ 2-3).

5) **Unpredictability of the art**. Cohen and Fauci (1998), highlights problems that have confounded treatment to date- HIV reside latent in cells in immunoprivelged sites, causes immunosuppression, destroys immune cells and continually mutates resulting in different strains in parts of the world. Hence treating HIV means that vaccines developed against one strain does not ensure treatment of other strains. As well, infected persons can harbor multiple forms o~" the virus. More specifically as it relates to the instant invention, Cohen and Fauci teach that treatment is affected by the lack of a vaccine. "Development of a safe and effective vaccine for HIV infection remains the "holy grail" of AIDS research". "The development of a safe and effective vaccine continues to encounter a host of sobering challenges, including geographic variability of HIV subtypes, and the lack of correlates of protective immunity in HIV infection." (page 88, col 1, ¶ 3). However, the instant claims recite use of CpG as an adjuvant. As neither the specification nor the state of the art demonstrate a potential vaccine that is effective, CpG cannot act as an adjuvant for treatment of HIV. Attempts to use CpG as a vaccine for HIV treatment demonstrated that CpG ineffective in producing positive results. Oehen et al (2000) found that DNA vaccination with CpG was not able to produce CTL protective responsive against infection

of a peripheral organ, which is the benchmark of treatment. As well, DNA vaccination was very short-lived and does not induce effector or memory CTL. Adverse effects accompany CpG administration. Schwartz et al have found that CpG motifs lead to inflammation in the lungs and contribute to disease progression and morbidity in some forms of lung disease (see e.g. page 68, col 1, ¶ 2).

6) **Summary**. The invention recites a method of enhancing the immune system in subjects with immune deficiency associated with HIV based upon demonstration of an enhancement IgM production, natural killer cells and IL-6 in uninfected mice. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of vaccines against HIV, the lack of a specific and well-established utility and the lack of guidance as to disease or biochemical targets provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1, 2, 87 and 88 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 37-43, 46-52, 56-61 and 91-101 of copending Application No. 11/296,644. **This is a new rejection necessitated by applicants' amendment.**

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of the instant invention are generic to all that is recited in claims as being unpatentable over claims 37-43, 46-52, 56-61 and 91-101 of copending Application No. 11/296,644. That is, the cited claims of U.S. Application No. 11/296,644 anticipate and fall entirely within the scope of the rejected claims of the instant application. Specifically, both applications recite a method of inducing an immune response in a subject with an immune deficiency associated with a viral infection using unmethylated CpG nucleic acids.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding the U.S. Application No. 11/296,644, then two different assignees would hold a patent to the claimed invention of U.S. Application No. 11/296,644, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 37-56 of copending Application No. 10/788,191 and claim 1, 2 and 88 over claims 37-65 of copending Application No. 11/067,516 and claims 1 and 2 over claims 19-33 of copending application 10/987146 and claims 1, 2 and 88 over claims 42-68 of copending application 10/382822. **These are new rejections.**

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite methods of administering an unmethylated CpG to a subject associated with HIV infection. The instant claims recite that administration results in a boost in the immune system, while the copending applications recite that the method treats the HIV infection. It would have been obvious to one of ordinary skill at the time of the invention was made to boost the immune system of the subject coordinate with the administration because the instant invention teaches that it is within the ordinary skill of the art to administer the CpG to subjects with HIV immune deficiency and because the copending applications teach that immune boost is critical to treatment of HIV infection. Based upon the teachings of the cited references,

the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding a patent from 10/788,191, 11/067,516, 10/987146, 10/382822 then several different assignees would hold a patent to the claimed invention of the copending applications, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Argument

It is acknowledged that applicants' will address the provisional obviousness double patenting rejections upon indication of allowable subject matter. However, until the recited claims are patented or a terminal disclaimer is filed, the claims remain rejected.

Conclusion

No Claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M Marvich

Maria B Marvich, PhD
Examiner
Art Unit 1633